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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/551,649	09/29/2005	Yechezkel Barenholz	BARENHOLZ9A	5688

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EXAMINER	
SHOMER, ISAAC	

ART UNIT	PAPER NUMBER
1612	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)
	10/551,649	BARENHOLZ ET AL.
	Examiner	Art Unit
	ISAAC SHOMER	1612

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 July 2011*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,6-8,10,11,13,14,16-20,26 and 81-85* is/are pending in the application.

4a) Of the above claim(s) *17-20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3, 6-8, 10, 11, 13, 14, 16, 26, and 81-85* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)	
1) ☒ Notice of References Cited (PTO-892)	4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)	5) ☐ Notice of Informal Patent Application
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.	6) ☐ Other: _____.

DETAILED ACTION

Applicants' arguments, filed 12 July 2011, have been fully considered. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claim Rejections - 35 USC § 112 2nd Paragraph – Maintained Rejections

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-3, 6-8, 10, 11, 13, 14, 16, 26, and 81-85 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The limitation "the components being selected such that he lipid assembly is chemically and physically stable under storage conditions of 4 [degrees Celsius] in biological fluids for at least six months" is indefinite. This is because it is unclear what is meant by "stable" for the reasons set forth below:

The specification provides details of four different tests conducted to determine stability, as of the section entitled "Stability of lipid assemblies comprising biologically active lipids" on pages 42 and 43 of the specification.

In applicant's arguments dated 12 July 2011 (hereafter referred to as applicant's arguments), applicant contends that claim 1 is definite, and that the skilled artisan would

have been aware as to what is meant by a stable liposome. Applicant explained the following regarding the chemical tests.

Chemical Stability Test A (pH): In regard to chemical stability test (a), applicant contends that any significant change from physiological pH is a sign of instability. Applicant quotes paragraph 0283 of the published specification (page 70, top paragraph) in support of this position.

This argument is not persuasive for the following reasons.

1. The claims do not recite that any significant deviation from physiological pH is a sign of instability.

2. The portion of the specification quoted by applicant does not define the term "stable" or "stability" in this manner.

3. If, purely *en arguendo*, the claims did recite that a significant change from physiological pH is a sign of instability, it is unclear what constitutes a significant change from physiological pH.

Chemical Stability Test B (hydrolysis): Applicant contends that in the example on page 70, first paragraph, of the specification, in this example, the amount of non-esterified fatty acids (abbreviated NEFA) did not increase above 3%. As such, applicant contends that any amount of fatty acids above 3% is evidence of instability.

This argument is not persuasive for the following reasons:

1. The claims do not recite that hydrolysis of greater than 3% is evidence of instability.

2. The portion of the specification quoted by applicant does not define the term "stable" or "stability" as comprising 3% hydrolysis or less.

Physical Stability Test A (Liposome Size): In this case, applicant cites paragraphs 0115-0116 of the published application. In this case, applicant contends that unstable systems have a tendency to aggregate or phase separate, wherein aggregation results in an increase in size. Applicant contends that a significant decrease in liposome size is also evidence of instability, as it is evidence of leakage of ceramide.

This argument is not persuasive for the following reasons:

1. The claims do not recite that a significant change in liposome size is evidence of instability.

2. The portion of the specification quoted by applicant does not define the term "stable" or "stability" in this manner.

3. Even if, purely *en arguendo,* the claims did define stability in terms of a significant change in liposome size, it is unclear what constitutes a "significant" change in size.

Physical Stability Test B (Free Ceramide): Applicant discloses that level of free, non-aggregated biologically active lipid is determined by TLC (thin layer chromatography). However, applicant does not disclose what levels of free lipid are required for the lipid assembly to be considered unstable. In response, applicant quotes MPEP 2173.02, which states that patentable subject matter must be disclosed with a reasonable degree of particularity and distinctness, and that some latitude in the

manner of expression and the aptness of the terms should be permitted. Applicant contends that a reasonable degree of distinctness is present in the instant case.

These arguments are not persuasive for the following reasons:

1. Applicant had no answers as to what levels of free ceramide is evidence of instability. Applicant further did not point to any sections from the specification defining the levels of free ceramide. Nor did applicant make any argument to the effect that the skilled artisan would have been aware of the levels of free ceramide that constitute instability.

Conclusion: Applicant has outlined four tests that determine stability. None of these tests are required by the claims or outlined in the specification. Furthermore, applicant has provided an answer as to liposomes that pass one stability test but fail another. For example, the skilled artisan would not have been apprised as to whether a liposome that has no significant change in pH upon storage, but incurs over 3% hydrolysis would have been stable. Similarly, the skilled artisan would not have been apprised of whether a liposome that incurs a significant change in size, but passes both chemical stability tests would have been considered stable. In light of this, the skilled artisan would not have been able to determine the metes and bounds of the term “stable” as used in claim 1.

Furthermore, applicant’s arguments support this rejection. Applicant’s arguments demonstrate that there are many different types of stability. It is not clear which type of stability, or which combination of types of stability, is required for a lipid assembly in order to meet the claimed invention.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1, 6-8, 10, 11, 13, 14, 16, 26, and 81-85 are rejected under 35 U.S.C. 103(a) as being unpatentable over Abra et al. (US Patent 6,126,966) in view of Igarashi et al. (US Patent 5,137,919).

Abra et al. (hereafter referred to as Abra) is drawn to a liposome composition comprising entrapped cisplatin, as of Abra, abstract. Said liposomes comprise a vesicle forming lipid, as well as a vesicle forming lipid derivatized with a hydrophilic polymer, as of Abra, column 21 lines 26-31, reading on components (b) and (c) of claim 1. Said vesicle forming lipid may be hydrogenated soy phosphatidylcholine (HSPC), and said derivatized vesicle forming lipid is distearyl phosphatidyl ethanolamine derivatized with polyethylene glycol (DSPE-PEG). Cisplatin is a known anti-tumor agent, as of Abra, column 1 lines 40-42.

Abra does not teach a biologically active, non-liposome forming lipid, as required by part (a) of claim 1.

Igarashi et al. (hereafter referred to as Igarashi) is drawn compounds having a profound effect on mammalian cell proliferation, as of Igarashi, column 1 lines 9-11. In one embodiment, Igarashi teaches the effect of N,N-dimethylsphingosine and N,N,N-trimethylsphingosine against cancer cells, as of Igarashi, column 2 lines 40-50 and

Figures 2A-2C, which show that both compounds have an effect against a cancer cell line.

It would have been prima facie obvious for one of ordinary skill in the art to have included the N,N-dimethylsphingosine, as of Igarashi, in the Abra. This is because N,N-dimethylsphingosine is taught to have an anti-cancer effect, as of Igarashi. Furthermore, the liposome of Abra is known for an anti-cancer use, as it comprises cisplatin, which is an anti-cancer drug. As such, the skilled artisan would have been motivated to have included N,N-dimethylsphigosine, which is an anti-cancer lipid as of Igarashi, into the liposome of Abra, to have predictably increase the anti-cancer effect in an additive manner. Generally, it is *prima facie* obvious to combine two compositions, each of which is taught by the prior art to be useful for same purpose (anti-cancer treatment), in order to form a third composition to be used for the very same purpose. The idea for combining them flows logically from their having been individually taught in the prior art. See MPEP 2144.06.

As to the stability test required by claim 1, Abra teaches stability tests regarding stability at 2-8 degrees Celsius for 6 months, as of Abra, column 10 Table 1, 9th line in table. In this case, Abra teaches that 99% of the platinum remained encapsulated after 6 months at 2-8 C. Furthermore, Abra teaches that liposomes which comprise DSPE-PEG have greater stability than liposomes lacking DSPE-PEG. This data is shown as of a test described by Abra, column 12, Table 3, in which a composition comprising DSPE-PEG had 95% encapsulated platinum at the end of the 2 week test period, whereas a

composition lacking DSPE-PEG had only 81% platinum encapsulated at the end of the same period.

As to claims 6-8, the N,N-dimethylsphingosine lipid of Igarashi reads on the lipid required by these claims.

As to claims 10-11, the lipopolymer used by Abra is DSPE-PEG. Said PEG may have a molecular weight of 120-20,000 Daltons, as of Abra, column 6 lines 13-14. This overlaps with the claimed size range of 2000 Daltons. While the prior art does not disclose the exact claimed values, but does overlap: in such instances even a slight overlap in range establishes a *prima facie* case of obviousness. In re Peterson, 65 USPQ2d 1379, 1382 (Fed. Cir. 2003).

As to claims 14 and 16, the hydrogenated soy phosphatidylcholine taught by Abra reads on the requirements of these claims.

As to claim 26, the composition of Abra is a pharmaceutical composition as it is used to deliver a drug. The liposomes are stored in aqueous solution; as such, Abra teaches that the liposomes may be combined with water, which is a pharmaceutical excipient.

As to claim 81, cisplatin, as taught by Abra, is the required therapeutic agnet.

As to claims 82-85, Abra suggests the inclusion of targeting molecules such as antibodies, antibody fragments, or cell-surface recognition molecules, which are attached by means of the hydrophilic chain to the derivatized lipid (e.g. DSPE-PEG-antibody). These targeting molecules would have been expected to associate with a biological target site, as they are taught by Abra for this purpose.

Claim 2 is rejected under 35 U.S.C. 103(a) as being unpatentable over Abra et al. (US Patent 6,126,966) in view of Igarashi et al. (US Patent 5,137,919) as applied to claims 1, 6-8, 10, 11, 13, 14, 16, 26, and 81-85 above, and further as evidenced by Kumar (Proc. Natl. Acad. Sci., Vol. 88, January 1991, pages 444-448).

Abra in view of Igarashi teach a liposome comprising a biologically active lipid, a lipopolymer, and a vesicle forming lipid, that is stable at about 4 C for six months.

The above references are silent with regard to the additive effective packing parameter of the liposome. Nevertheless, the prior art teaches a liposome, and liposomes are known to have a bilyer. Kumar provides evidence that a lipid assembly that comprises a bilayer has an additive packing parameter of 0.74 or greater, as of Kumar, page 447, left column, first paragraph of discussion section. As such, the skilled artisan would have understood that the additive packing parameter of the liposome of the prior art would have been 0.74 or greater.

Claim 3 is rejected under 35 U.S.C. 103(a) as being unpatentable over Abra et al. (US Patent 6,126,966) in view of Igarashi et al. (US Patent 5,137,919) as applied to claims 1, 6-8, 10, 11, 13, 14, 16, 26, and 81-85 above, and further as evidenced by Tirosh et al. (Biophysical Journal, Vol. 74, March 1998, pages 1371-1379).

Abra in view of Igarashi teach a liposome comprising a biologically active lipid, a lipopolymer, and a vesicle forming lipid, that is stable at about 4 C for six months.

The above references are silent with respect to the number of water molecules bound to the lipopolymer headgroup. However, the lipopolymer headgroup is polyethylene glycol (PEG), with a molecular weight of at between 120-20,000 Daltons, as of Abra. The skilled artisan would have expected that in the hydrated state, a PEG moiety with a molecular weight of 2000 would have comprised at least 60 water molecules per headgroup. Evidence for this is provided by Tirosh et al. (hereafter referred to as Tirosh). Tirosh teaches that the hydration number of PEG is about 136, which is understood to read on the fact that there are at least 136 water molecules per PEG moiety, as of Tirosh, page 1373, right column Table 1. As such, the skilled artisan would have understood that the PEG groups in the liposome of the prior art tightly bind at least 60 water molecules, as required by claim 3.

Claims 1, 6-8, 10, 11, 13, 14, 16, 26, and 81-85 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pietzyk et al. (International Journal of Pharmaceutics, Vol. 196, 2000, pages 215-218) in view of Drummond et al. (Pharmacological Reviews, Vol. 51, No. 4, 1999, pages 691-743) and Igarashi et al. (US Patent 5,137,919).

Pietzyk et al. (hereafter referred to as Pietzyk) is drawn to liposomes comprising the anti-cancer drug carboplatin, as of Pietzyk, page 215, abstract. Said liposomes were tested by storage for 6 months in the refrigerator, as of Pietzyk, page 215, abstract. In one embodiment, Pietzyk tests various liposomes for stability, including liposomes

composed only of phosphatidylcholine (reading on lipid (c) of claim 1), as of Pietzyk, page 216, Table 1 (reproduced below), specifically the first column of the table.

Storage conditions	Content of PC, LPC and PE (mol%) in liposomes consisting of			
	PC	PC + Ch	PC + AP[a,b]	PC + Ch + AP[a,b]
4°C and darkness	PC 94.6 LPC 5.4 PE 0.0	PC 100 LPC 0.0 PE 0.0	PC 60.0 LPC 11.0 PE 5.0	PC 65.3 LPC 12.0 PE 5.0
Room temperature and day light	PC 85.8 LPC 14.2 PE 0.0	PC 100 LPC 0.0 PE 0.0	PC 19.0 LPC 59.6 PE 5.0	PC 21.5 LPC 58.1 PE 5.0

[a] The difference to 100% consists of water soluble compounds which were separated during preparation of the samples for HPLC.
[b] pH of the liposome preparation: 3.5–4.0

The phosphatidylcholine used by Pietzyk is fully hydrogenated, as of Pietzyk page 215, right column, last paragraph. In another embodiment, Pietzyk teaches a liposome that comprises cholesterol, as of Pietzyk, page 216, Table 1, second column of the table.

Pietzyk does not teach a non-liposome forming lipid that reads on part (a) of claim 1. Pietzyk does not teach a lipopolymer that reads on part (b) of claim 1.

Drummond et al. (hereafter referred to as Drummond) is drawn to liposomes for delivery of drugs to tumors (i.e. cancer sites), as of Drummond, page 691, title. Drummond, page 725 part VII is drawn to stability of liposomes in plasma and storage. Drummond, page 728 right column, paragraph numbered 5, teaches that the presence of PEG on the surface of the liposome provides a steric barrier that prevents liposome aggregation, and liposomes are stable for many months to years when stored below the phase transition temperature of the phosphatidylcholine component. Drummond suggests the use of a PEG-ceramide (as opposed to PEG-DSPE) to avoid some of the

problems of PEG-DSPE regarding stability, as of Drummond, page 727, right column, last line, and first two lines on page 728.

It would have been prima facie obvious for one of ordinary skill in the art to have included PEG-ceramide, as of Drummond, in the liposome of Pietzyk. This is because PEG-ceramide is known to increase liposomal stability with regard to aggregation. Furthermore, PEG-ceramide appears to avoid some of the problems of PEG-DSPE. As such, the skilled artisan would have been motivated to have included PEG-ceramide to have predictably increased stability with regard to aggregation with a reasonable expectation of success.

Neither Pietzyk nor Drummond teach a lipid that reads on lipid (a) of claim 1, as the PEG-ceramide of Drummond reads on lipopolymer (b) but not lipid (a).

Igarashi et al. (hereafter referred to as Igarashi) is drawn compounds having a profound effect on mammalian cell proliferation, as of Igarashi, column 1 lines 9-11. In one embodiment, Igarashi teaches the effect of N,N-dimethylsphingosine and N,N,N-trimethylsphingosine against cancer cells, as of Igarashi, column 2 lines 40-50 and Figures 2A-2C, which show that both compounds have an effect against a cancer cell line.

It would have been prima facie obvious for one of ordinary skill in the art to have included the N,N-dimethylsphingosine, as of Igarashi, in the liposome of Pietzyk and Drummond. This is because N,N-dimethylsphingosine is taught to have an anti-cancer effect, as of Igarashi. Furthermore, both the liposomes of Pietzyk and Drummond are drawn to anti-cancer treatment, as the liposome of Pietzyk includes carboplatin (an anti-

cancer drug), and Drummond teaches anti-tumor liposomes in its title. As such, the skilled artisan would have been motivated to have included N,N-dimethylsphigosine, as of Igarashi, into the liposome of Pietzyk and Drummond, to have predictably increase the anti-cancer effect in an additive manner. Generally, it is *prima facie* obvious to combine two compositions, each of which is taught by the prior art to be useful for same purpose (anti-cancer treatment), in order to form a third composition to be used for the very same purpose. The idea for combining them flows logically from their having been individually taught in the prior art. See MPEP 2144.06.

As to the stability test of claim 1, the skilled artisan would have expected that the liposome of the combined references would have been stable throughout applicant's claimed time period. This is because the liposome of Pietzyk comprises only saturated (i.e. hydrogenated) phosphatidylcholines, as of Pietzyk, page 215, right column. The choice of a saturated phospholipid component is essential in maintaining stability, as of Drummond, page 726, right column, 19th line of top paragraph. Furthermore, said liposome includes a PEG-ceramide, which is important for maintaining stability, as of Drummond, page 728, section 5.

As to claims 6-8, the lipid N,N-dimethylsphingosine, as of Igarashi, reads on the lipids recited by this claim.

As to claim 10, Drummond clearly teaches a lipid modified with polyethylene glycol (PEG). As to claim 11, a molecular weight of 5000 Daltons appears to be most preferred, as of Drummond, page 727, right column, last paragraph, 7th line from

bottom. However, as to claim 13, a molecular weight of 2000 Daltons also appears to be acceptable.

As to claim 16, Pietzyk teaches a liposome made from phosphatidylcholine.

As to claim 81, Pietzyk teaches the incorporation of carboplatin, as of Pietzyk, abstract, whereby carboplatin is an anti-cancer drug. Drummond further teaches doxorubicin, which is also an anti-cancer drug, as of Drummond, page 730 left column, part A.

As to claims 26 and 82-85, Drummond teaches active targeting of liposomes, as of Drummond, page 730, right column, part B. Said targeting ligands may be via small molecules, sugars, serum proteins, antibodies, or antibody fragments.

Claim 2 is rejected under 35 U.S.C. 103(a) as being unpatentable over Pietzyk et al. (International Journal of Pharmaceutics, Vol. 196, 2000, pages 215-218) in view of Drummond et al. (Pharmacological Reviews, Vol. 51, No. 4, 1999, pages 691-743) and Igarashi et al. (US Patent 5,137,919) as applied to claims 1, 6-8, 10, 11, 13, 14, 16, 26, and 81-85 above, and further as evidenced by Kumar (Proc. Natl. Acad.S ci., Vol. 88, January 1991, pages 444-448).

Pietzyk in view of Drummond and Igarashi is drawn to a liposome comprising phosphatidylcholine, N,N-dimethylsphingosine, and PEG-ceramide. See the above rejection under Pietzyk, Drummond, and Igarashi.

The above references are silent with regard to the additive effective packing parameter of the liposome. Nevertheless, the prior art teaches a liposome, and

liposomes are known to have a bilyer. Kumar provides evidence that a lipid assembly that comprises a bilayer has an additive packing parameter of 0.74 or greater, as of Kumar, page 447, left column, first paragraph of discussion section. As such, the skilled artisan would have understood that the additive packing parameter of the liposome of the prior art would have been 0.74 or greater.

Claim 3 is rejected under 35 U.S.C. 103(a) as being unpatentable over Pietzyk et al. (International Journal of Pharmaceutics, Vol. 196, 2000, pages 215-218) in view of Drummond et al. (Pharmacological Reviews, Vol. 51, No. 4, 1999, pages 691-743) and Igarashi et al. (US Patent 5,137,919) as applied to claims 1, 6-8, 10, 11, 13, 14, 16, 26, and 81-85 above, and further as evidenced by Tirosh et al. (Biophysical Journal, Vol. 74, March 1998, pages 1371-1379).

Pietzyk in view of Drummond and Igarashi is drawn to a liposome comprising phosphatidylcholine, N,N-dimethylsphingosine, and PEG-ceramide. See the above rejection under Pietzyk, Drummond, and Igarashi.

The above references are silent with respect to the number of water molecules bound to the lipopolymer headgroup. However, the lipopolymer headgroup is polyethylene glycol (PEG), with a molecular weight of at least 2000 Daltons, as of Drummond. The skilled artisan would have expected that in the hydrated state, a PEG moiety with a molecular weight of 2000 would have comprised at least 60 water molecules per headgroup. Evidence for this is provided by Tirosh et al. (hereafter referred to as Tirosh). Tirosh teaches that the hydration number of PEG is about 136,

which is understood to read on the fact that there are at least 136 water molecules per PEG moiety, as of Tirosh, page 1373, right column Table 1. As such, the skilled artisan would have understood that the PEG groups in the liposome of the prior art tightly bind at least 60 water molecules, as required by claim 3.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ISAAC SHOMER whose telephone number is (571)270-7671. The examiner can normally be reached on 8:00 AM - 5:00 PM Monday-Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Frederick F. Krass can be reached on (571)272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/ISAAC SHOMER/
Examiner, Art Unit 1612

/Frederick Krass/
Supervisory Patent Examiner, Art Unit 1612